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The application of the Auer-Kleiner morphine test in human diabetes.By **ALBERT A. EPSTEIN.***[From the Mt. Sinai Hospital, New York City.]*

Auer-Kleiner¹ have found that the administration of morphine of definite dosage to dogs, in which the pancreas had been injured experimentally, caused a very marked rise in the blood sugar, lasting several hours. The administration of opium and its derivatives in the treatment of diabetes mellitus has been a common practice for many years. Many noted observers ascribe beneficial results to this agent. Even today opiates are commonly used in diabetes, particularly in painful conditions, which often complicate this disease.

The observations of Auer and Kleiner are therefore of interest and importance, not only from the standpoint that the administration of morphine to diabetic suspects might (in a very simple manner) give a clue as to the existence of the disease, but they would throw light also on two other phases; namely, (1) the relation of glycosuria to pancreatic disorders; (2) the effect of morphine on the course of the hyperglycemia in diabetes. In other words, if morphine is capable of superinducing a hyperglycemia in animals with pancreatic injury, the increase of a hyperglycemia after the use of morphine in a diabetic individual or its development in a diabetic suspect, would indicate, on the one hand, that a pancreatic disturbance is present; on the other, that the beneficial effects of morphine (as regards pain, etc.) are accompanied by undesirable developments.

I have applied this test in a number of diabetics, both in the sugar-free and the glycosuric states, with the object of determining whether or not the results obtained in experimental animals occur in the human being. The dose of morphine used, given hypodermically, was $\frac{1}{4}$ of a grain (0.015 g.). This dose is relatively small compared to that used by Auer and Kleiner, in their experiments on dogs; but it is the maximum dose that I felt justified

¹ Auer and Kleiner, PROC. SOC. EXP. BIOL. AND MED., XV, 1, p. 2, 1917.

in administering to patients. The other conditions of the test were like those observed by Auer and Kleiner. The tests were conducted in the following manner: The patients were kept in bed, and after a night of rest and fasting were given a cup of black coffee early in the morning; no other food was given. At noon a specimen of the patient's blood was taken for blood sugar analysis; another at 12.30; a third, at one o'clock; and two others, at hourly intervals. This constituted the control day, as no morphine was given. At the end of this period, the patient received food. On the following day, the tests were made in exactly the same order, with the addition that directly after the removal of the first specimen of blood, a dose of morphine was given. The accompanying chart shows the maximum and minimum effects produced by the morphine. It is evident that in the case showing the maximum change (Example 1) a certain elevation of the blood sugar occurs. This elevation, however, is very slight, compared to the changes observed by Auer and Kleiner in dogs. The rise here observed would not be sufficient to base the conclusion that a mobilization of sugar occurred in consequence of the morphine administration. In a majority of the cases observed, the change in the hyperglycemia was even less marked than this. The other case presented (Example 2) shows the course of the hyperglycemia before and after the administration of the morphine. In this instance, as in many others, the morphine is without any effect at all.

The results of the observations which I present here do not in any way militate against the results obtained by Auer and Kleiner in their experiments. The discrepancy may be due to a difference in the size of the dose (per kilogram body weight) of morphine used in the tests made by Auer and Kleiner, and those made by me. It is questionable whether the method can have the clinical application which was expected, unless one desires to exceed the rules of therapeutic usage, in regard to the morphine. The effect of the morphine upon all the patients tested was pronouncedly narcotic.

I have intentionally omitted to discuss the question of the effect of morphine on the glycosuria because the results were too variable to admit of any conclusions.

MORPHINE TEST.

Blood Sugar.

Time.	Per Cent.			
	Example I.		Example II.	
	Control Day.	Test Day.	Control Day.	Test Day.
12.00	0.180	0.180	0.156	0.150
12.30	0.182	0.202	0.132	0.135
1.00	0.182	0.216	0.135	0.140
2.00	0.176	0.180	0.135	0.128
3.00	0.180	0.179	0.138	0.123

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A method for determining minute quantities of nitrogen in nitrogenous substances.

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When an alkaline mixture containing phenol and NH_3 or NH_2 groups is oxidized by a hypochlorite, a blue-colored solution results. This color is produced in the cold in mixtures of proper concentration, while mixtures of more dilute solutions give no color or only a very faint blue. Upon heating the mixtures, those containing the minutest trace of the above-mentioned groups develop a color, while the color of the more concentrated ones deepens considerably in intensity. The latter varies in direct proportion to the amount of the NH_3 and amino acid group present.

This reaction is made the basis of colorimetric methods for the estimation of incoagulable nitrogen, urea and ammonia nitrogen in blood, urine and other biological fluids, and for the estimation of certain substances containing amino groups such as albumen, arsphenamin (salvarsan), etc. The estimation is carried out by comparison with a suitable set of standards or in a colorimeter against a known standard.

In estimating incoagulable nitrogen of the blood, the method briefly is as follows: the proteids are precipitated either by the addition of 2.5 per cent. trichloracetic acid to 10 times the volume